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Inside This Issue

STATE-OF-THE-ART PAPER

Bonaca and colleagues review the optimal combinations of antithrombotic therapies, their timing, and the appropriate targeted subgroups to produce maximal thrombotic efficacy while reducing the risk of hemorrhagic complications in patients with acute coronary syndromes (ACS). The efficacy and safety data for the most commonly used drugs are reviewed including heparins, glycoprotein IIb/IIIa inhibitors, antithrombins, factor Xa inhibitors, and antiplatelet agents. Integrating the new data into treatment guidelines is complicated by different efficacy and safety end points and the variability in study populations and presenting syndromes. In many situations there is a lack of data, or conflicting data, leading to questions and controversies that will hopefully be resolved when the results of ongoing trials are available.

VIEWPOINT

In a viewpoint paper, Dove, Weaver, and Lewin address proposals currently being reviewed by Congress to create a more integrated health care delivery system. Such a system has the potential to reduce, or at least constrain, medical costs by reducing duplication of diagnostic procedures and potentially by changing provider reimbursement from procedure- or service-based to capitation-based. Accountable care organizations (ACOs) is the terminology for these integrated systems. The ACO structure is complicated; it appears to require partnerships between hospitals and physicians, raising concerns that hospital-led ACOs will force physician employment by hospitals. The authors argue that patients, physicians, and payers are in a better position to guide the redesign of the health care delivery system than government agencies, policy organizations, or elected officials. They conclude with the statement: "We strongly believe—and the ACC has proclaimed—that change in health care delivery must be accomplished with patients and physicians at the table."

(continued on page A-20)

CLINICAL RESEARCH

CLINICAL TRIAL

Monaco and colleagues randomized over 200 patients scheduled for elective surgical treatment of major vascular disease to either a standard pre-operative evaluation, where coronary angiography was performed based on the results of noninvasive tests, or a systematic strategy, where all patients underwent pre-operative coronary angiography. Both groups were revascularized as needed, and surgery was delayed for at least 30 days in those who underwent either bare-metal stenting or bypass surgery. Nearly 60% of the systematic group was revascularized prior to the surgery, compared with 40% in the standard group. The in-hospital major adverse cardiovascular event rate was slightly, but not significantly, lower in the mandatory group. However, at 5 years there was a significant reduction in mortality in those who were mandated to angiography. In this study, a strategy of routine coronary angiography positively impacted long-term outcomes in patients referred for vascular surgery.

Editorial Comment: Giora Landesberg, Morris Mosseri, p. 997

HEART RHYTHM DISORDERS

Prolonged longevity is leading to an increased need for stroke prevention in atrial fibrillation (AF) patients age ≥80 years, but the safety in very elderly patients has been questioned. Poli and colleagues conducted a prospective observational study on 783 AF patients on oral anticoagulant treatment (OAT) at a single clinic devoted to the management of OAT. Patients spent a median of 14%, 71%, and 15% time below, within, and above the intended therapeutic range, respectively. No difference in OAT quality was found between patients age <80 and ≥80 years. The overall rate of major bleeding complications was 1.4 per 100 patient/years. Patients age >80 years were twice as likely to have bleeding complications. These results indicate that the rate of major bleeding complications is higher in very elderly AF patients on OAT, but can be kept reasonably low if careful management of anticoagulation is obtained.

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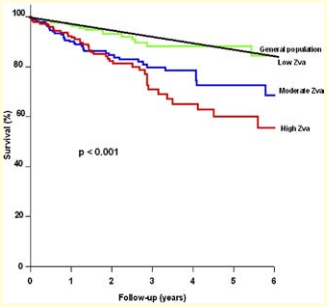
VALVULAR HEART DISEASE

Calculating Z_{Va} Improves Risk Stratification in Patients With AS 1003



Zeineb Hachicha, Jean G. Dumesnil, Philippe Pibarot

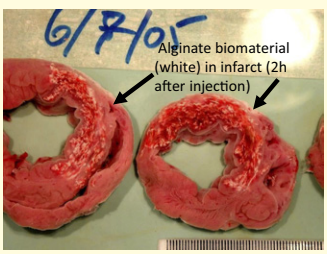
This study by Hachicha and colleagues examined the prognostic value of valvuloarterial impedance (Z_{va}) in patients with aortic stenosis (AS). Z_{va} estimates the global hemodynamic load faced by the left ventricle (LV) and is calculated by dividing the estimated LV systolic pressure (systolic arterial pressure + mean transvalvular gradient) by the stroke volume indexed for the body surface area. Over 500 asymptomatic patients with at least moderate AS (aortic jet velocity $\geq$2.5 $m \cdot s^{-1}$) were followed for total mortality, regardless of the realization of aortic valve replacement. Four-year survival was significantly lower in the patients with a baseline Z_{va} $\geq$4.5 mm $Hg \cdot ml^{-1} \cdot m^2$ compared with those with Z_{va} between 3.5 and 4.5 mm $Hg \cdot ml^{-1} \cdot m^2$ and those with Z_{va} $\leq$3.5 mm $Hg \cdot ml^{-1} \cdot m^2$. Increased Z_{va} is a marker of excessive LV hemodynamic load and may be useful to improve risk stratification and clinical decision making in patients with AS.

Editorial Comment: Helmut Baumgartner, Catherine M. Otto, p. 1012

PRE-CLINICAL RESEARCH

PRE-CLINICAL RESEARCH

Injectable Hydrogel May Limit Post-MI Remodeling 1014



Jonathan Leor, Shmuel Tuvia, Victor Guetta, Ferenc Manczur, David Castel, Udi Willenz, Örs Petnehâzy, Natali Landa, Micha S. Feinberg, Eli Konen, Orly Goitein, Orna Tsur-Gang, Mazal Shaul, Lea Klapper, Smadar Cohen

This study tested the hypothesis that a hydrogel injected into the infarct-related artery a few days post-infarction could constrain the myocardium from expanding, thereby limiting left ventricular (LV) remodeling by providing temporary physical support to the damaged cardiac tissue. Leor and colleagues prepared a calcium cross-linked alginate solution that undergoes liquid to gel phase transition. In a swine model of anterior myocardial infarction (MI), alginate solution or saline was injected selectively into the infarct-related coronary artery. Examination of hearts harvested after injection showed that the alginate crossed the infarcted endothelium and was deposited as hydrogel in the infarcted tissue. This prevented and even reversed the LV enlargement seen in control animals. Further experiments showed that the material did not provoke thrombotic complications either locally or remotely. These results suggest that intracoronary injection of alginate biomaterial may prevent adverse remodeling after MI.

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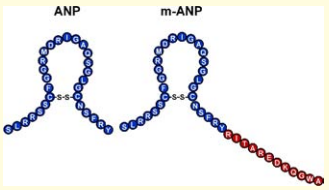

PRE-CLINICAL RESEARCH

ANP Gene Mutation Results in a Novel Peptide With Useful Cardiovascular and Renal Effects **1024**

Paul M. McKie, Alessandro Cataliotti, Brenda K. Huntley, Fernando L. Martin, Timothy M. Olson, John C. Burnett, Jr

The cardiac hormone atrial natriuretic peptide (ANP) is a 28-amino acid (AA) peptide that consists of a 17-AA ring structure together with a 6-AA N-terminus and a 5-AA C-terminus. A mutation in the gene was identified from a cohort with familial atrial fibrillation, which produces a 40-AA peptide consisting of native ANP (1-28) and a C-terminal extension of 12 AA. McKie and colleagues named this peptide mutant atrial natriuretic peptide (mANP), and herein report on its physiologic actions. In cultured cardiac fibroblasts, ANP and mANP produced incremental increases in 3′,5′-cyclic guanosine monophosphate. In a dog model, high-dose mANP produced significantly greater diuretic, natriuretic, renin-angiotensin-aldosterone system inhibiting, cardiac unloading, and blood pressure-lowering properties compared with native ANP. These results suggest that mANP exerts greater and more sustained natriuretic, diuretic, glomerular filtration rate, and renal blood flow-enhancing actions than native ANP.

Editorial Comment: Adolfo J. de Bold, p. 1033